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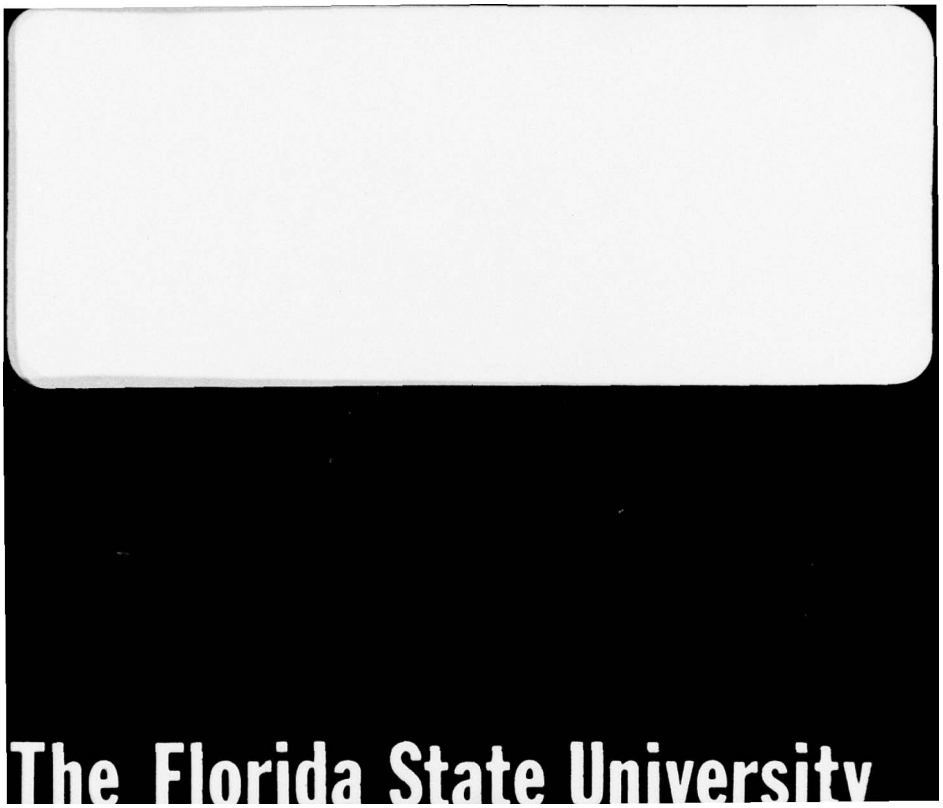
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by

(10) Susan L. Conlon [redacted] L. Billard

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THE MEAN DURATION TIME OF CARRIER-BORNE EPIDEMICS

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ABSTRACT

In this paper, the two-population model for a carrier-borne epidemic posed by Bailey (The Mathematical Theory of Infectious Diseases and its Applications, 1975, p. 211) is formulated in a mathematically tractable manner. This model reflects the epidemiology of diseases such as malaria, where the progress of the disease depends on the interaction of a population of mosquitoes and a population of humans. An expression for the mean duration time of the epidemic is obtained and a computationally feasible algorithm is presented. Results of a study investigating the consequences on the mean duration time of varying the infection and removal rates in the two populations are given.

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KEYWORDS: carrier-borne epidemic, malaria, mean duration time

1. INTRODUCTION

In the theory of epidemic processes developed thus far, it has generally been assumed, in the simplest case, that the population of interest is closed and may be divided into sub-populations whose members may be classified as susceptible or infective. A slightly more complicated model introduces a third sub-population of removals.

These simple models and the associated theory are inadequate in the study of several diseases (malaria, for example) in which the spread of the disease by carriers is a recognized phenomenon. A carrier is an individual who may transmit the disease to other individuals, but who has no overt disease symptoms himself.

In the first significant work in this area, Weiss (1965) considers a closed population of m susceptibles, into which n carriers are initially introduced. There is no subsequent introduction of carriers, nor do any susceptibles become carriers during the course of the epidemic. The carriers are detectable only by the discovery of infected persons, and the epidemic progresses until either all susceptibles become infected or all carriers are removed.

Several extensions to the Weiss model have been considered. Downton (1968) allows for the further creation of carriers from the susceptibles during the course of the epidemic. Dietz and Downton (1968) relax the assumption of a closed population and allow for immigration of susceptibles and/or carriers. Pettigrew and Weiss (1967) consider an epidemic involving two types of infectives (e.g., clinically infected and sub-clinically infected individuals) in an infinite population of susceptibles. Applying results from branching processes, they obtain equations for the mean number of clinically infected individuals and for the mean number of sub-clinically infected individuals (carriers) at any time t.

Our concern, however, is not with the one-population model of these authors, but rather with the two-population model as discussed by Bailey (1975, p. 211). This permits consideration of such carrier-borne epidemics as malaria, in which the carriers (mosquitoes) form a population distinct from the host population (humans).

In Section 2 of this paper, we present a stochastic model for the two-population carrier-borne epidemic. A theoretical expression for the mean duration time is derived in Section 3 and a computationally feasible algorithm, based on a recursion relation, is presented in Section 4. In the final section, we present some numerical results for selected parameter values.

2. THE CARRIER-BORNE EPIDEMIC MODEL

Let $S_j(t)$, $I_j(t)$, and $R_j(t)$ denote the number of susceptibles, infectives, and removals, respectively, in population j at time t. Population j is of fixed size

$$N_j = S_j(t) + I_j(t) + R_j(t),$$

j = 1,2, for all t. The subscript j = 1 will refer to the host population and j = 2 will refer to the carrier population. Let $\underset{\sim}{Z}(t) = (S_1(t),I_1(t); S_2(t),I_2(t))$ have realization $\underset{\sim}{z}(t) = \underset{\sim}{z} = (s_1,i_1; s_2,i_2)$. Then $\underset{\sim}{z}$ takes values in the state space

$$A = \{\underset{\sim}{z} = (s_1,i_1; s_2,i_2): 0 \le s_j,i_j \le N_j; 0 \le s_j + i_j \le N_j, j=1,2\}.$$

Note that, since $R_j(t) = N_j(t) - S_j(t) - I_j(t)$, we need not include the number of removed individuals in the definition of $\underset{\sim}{Z}(t)$.

In a simplification of the epidemiology of malaria, a human susceptible acquires infection through being bitten by an infective female mosquito. The parasites released by the mosquito multiply in the liver of the human host, and then settle in the red blood cells. Female mosquitoes, seeking the blood required for the development of their eggs, are then infected by biting an infected human host. Thus, the probability that an additional human susceptible becomes infected during a short time interval is proportional to the number of human susceptibles, the number of infected carriers, and the length of the time interval. Similarly, the probability an additional carrier becomes infected during a short time interval is proportional to the number of susceptible carriers, the number of infected humans, and the length of the time interval. The removal rates are assumed linear.

Thus, the probabilities of permissible transitions in the interval (t,t+dt) are:

(i) $P\{(s_1,i_1;s_2,i_2) \to (s_1-1,i_1+1;s_2,i_2)\} = \beta_1 s_1 i_2 dt + o(dt)$,

(ii) $P\{(s_1,i_1;s_2,i_2) \to (s_1,i_1-1;s_2,i_2)\} = \gamma_1 i_1 dt + o(dt)$,

(iii) $P\{(s_1,i_1;s_2,i_2) \to (s_1,i_1;s_2-1,i_2+1)\} = \beta_2 s_2 i_1 dt + o(dt)$,

(iv) $P\{(s_1,i_1;s_2,i_2) \to (s_1,i_1;s_2,i_2-1)\} = \gamma_2 i_2 dt + o(dt)$,

and

(v) $P\{(s_1,i_1;s_2,i_2) \to (s_1,i_1;s_2,i_2)\} = 1-(\beta_1 s_1 i_2 + \gamma_1 i_1 + \beta_2 s_2 i_1 + \gamma_2 i_2)dt + o(dt)$,

where β_j and γ_j, the infection and removal rates, respectively, are assumed constant.

3. MEAN DURATION TIME

Our epidemic process is said to be terminated whenever no more human susceptibles can acquire infection. This occurs when one or more of the following subsets of A is entered, viz.,

E_1: the number of human susceptibles is zero,

E_2: the number of infectives in each population is zero,

and

E_3: there are no susceptible or infective carriers (i.e., all carriers have been removed).

Then, let

$$B = E_1 \cup E_2 \cup E_3,$$

where, from the definitions above,

$$E_1 = \{(0,i_1;s_2,i_2)\},$$

$$E_2 = \{(s_1,0;s_2,0)\},$$

and

$$E_3 = \{(s_1,i_1;0,0)\}.$$

Let the complement of the set B be

$$G = A-B.$$

Now, we are interested in T_m, the mean time required for an epidemic which is currently in state $m \in G$ to enter a state in the set B.

To derive expressions for the mean duration time, we consider our process as a continuous time Markov chain with a one-dimensional state space. In order to identify each vector in A by a natural number, we apply the transformation

$$k \equiv k(s_1,i_1;s_2,i_2)$$

$$= \epsilon(N_{1+}-N_{2+})\{s_1(N+1)N/2 + N_{2+}(N_{2+}+1)/2\}$$

$$+ \binom{N+1}{2}^2 + (N_{1+}+1)N_{1+}(N+1)/2 + (N+1)s_1 + (s_2+1),$$

where

$$N_{j+}=s_j+i_j, j=1,2;\ N=\max(N_{1+},N_{2+}) \text{ and } \epsilon(x) = I(x \geq 0).$$

The transformed state space is

$$A_T = \{h: 1 \leq h \leq \binom{N_1+2}{2}\binom{N_2+2}{2},\ h \text{ integer}\}.$$

For example, the first nine states in A_T, regardless of the population sizes, are:

$\underset{\sim}{z}$	$k(\underset{\sim}{z})$
(0,0;0,0)	1
(0,0;0,1)	2
(0,0;1,0)	3
(0,1;0,0)	4
(0,1;0,1)	5
(0,1;1,0)	6
(1,0;0,0)	7
(1,0;0,1)	8
(1,0;1,0)	9

We note that there is a unique one-to-one correspondence between the vectors in A and the integers in A_T. An algorithm to determine the vector in A which corresponds to a given $h \in A_T$ is presented in Conlon (1977).

In this transformed state space, we define the transition probabilities to be:

$$p_{mn}(t) = P[h(t) = n | h(o) = m]$$
$$= P[h(t + s) = n | h(s) = m]$$
$$= \nu_{mn} t + o(t),$$

$$p_{mm}(t) = 1 - \nu_m t + o(t),$$

where

$$\nu_m = \sum_{\substack{n \in A_T \\ n \neq m}} \nu_{mn},$$

and h(t) denotes the state the epidemic is in at time t. The hazard rates for the epidemic process are

$$\nu_{mn} = \begin{cases} \beta_1 s_1 i_2, & n=k_1=k(s_1-1,\ i_1+1;\ s_2,\ i_2) \\ \gamma_1 i_1, & n=k_2=k(s_1,\ i_1-1;\ s_2,\ i_2) \\ \beta_2 s_2 i_1, & n=k_3=k(s_1,\ i_1;\ s_2-1,\ i_2+1) \\ \gamma_2 i_2, & n=k_4=k(s_1,\ i_1;\ s_2,\ i_2-1) \end{cases}$$

Thus,

$$\nu_m = \beta_1 s_1 i_2 + \gamma_1 i_1 + \beta_2 s_2 i_1 + \gamma_2 i_2.$$

A Markov chain is said to be uniformizable if $\sup_m \nu_m = \nu_o < \infty$. Since our chain is finite, uniformizability follows immediately. Keilson (1974) showed that the original process (our uniformizable chain) and a discrete-time process constructed by randomly selecting the number of transitions according to a Poisson process with parameter ν_o have state probabilities identical in law.

For some $\nu \geq \nu_o$, let

$$a_{mn} = \begin{cases} \nu_{mn}/\nu, & m \neq n \\ 1 - \nu_m/\nu, & m = n, \end{cases}$$

and

$$A_\nu = \langle a_{mn} \rangle .$$

Then, following Keilson (1974), we can derive the consistency relation

$$\underline{\mu} = (T_m) = \frac{1}{\nu}[I_G - A_{\nu,G}]^{-1} \underset{\sim}{1}_G, \tag{3.1}$$

where $A_{\nu,G}$ is the matrix A_ν restricted to the good states.

To illustrate the theory, let us consider the first nine states of an epidemic, as presented above. If we choose β_1=0.1, β_2=0.2, γ_1=0.2, and γ_2=0.2, then the ν_m are given by

m	1	2	3	4	5	6	7	8	9
ν_m	0	0.2	0	0.2	0.4	0.4	0	0.3	0

Thus, $\nu_o = \max_m \nu_m = 0.4$. Let $\nu = 1$. Then the matrix $A_{\nu=1}$ is

$$A_1 = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ .2 & .8 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ .2 & 0 & 0 & .8 & 0 & 0 & 0 & 0 & 0 \\ 0 & .2 & 0 & .2 & .6 & 0 & 0 & 0 & 0 \\ 0 & 0 & .2 & 0 & .2 & .6 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & .1 & 0 & .2 & .7 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

We observe that G consists of the state corresponding to h=8 only. Thus, $A_{1,G}$=0.7, a scalar, and the consistency equation (3.1) gives the mean duration time of an epidemic which is currently in state (1,0;0,1):

$$T_8 = (1-0.7)^{-1} \cdot 1 = 3.\overline{3}.$$

We note that the choice of $\nu \geq \nu_o$ is arbitrary. If, for example, we choose $\nu = 2$, we have

$$T_8 = \tfrac{1}{2}(1-.85)^{-1} \cdot 1 = 3.\overline{3}.$$

In general, when more good states are considered, the dimension of $A_{\nu,G}$ is quite large, and the inversion of $[I_G - A_{\nu,G}]$ is cumbersome. For example, in the situation where $N_{1+} = N_{2+} = 8$, there are 2025 states in the transformed state space A_T, with 505 states in B and 1520 states in G. A computationally feasible algorithm is required.

4. A RECURSION APPROACH

In the previous section, we presented the consistency equation for T_m, together with the relevant theoretical justifications. We also noted potential difficulties in actually computing values for T_m when the population sizes are not small. We comment here on a computationally feasible (and easily programmable) approach to the calculation of T_m.

We observe that the mean duration time of our epidemic process at any given state can be decomposed into the sum of the following components: the average time spent in the given state, and the weighted mean duration times of the epidemic in those states to which the epidemic may proceed in one step from the given state. The weights are the hazards of each permissible one-step transition from the given state. Thus, if we let $T(s_1,i_1;s_2,i_2)$ denote

the mean duration time of an epidemic which is currently in state $(s_1,i_1;s_2,i_2)$, we may write the following recursion relation:

$$T(s_1,i_1;s_2,i_2)$$

$$= \frac{1}{\nu(s_1,i_1;s_2,i_2)} \Big[1 + \beta_1 s_1 i_2 \, T(s_1-1,i_1+1;s_2,i_2) + \gamma_1 i_1 \, T(s_1,i_1-1;s_2,i_2) + \beta_2 s_2 i_1 \, T(s_1,i_1;s_2-1,i_2+1) + \gamma_2 i_2 \, T(s_1,i_1;s_2,i_2-1)\Big],$$

where $\nu(s_1,i_1;s_2,i_2) = \beta_1 s_1 i_2 + \gamma_1 i_1 + \beta_2 s_2 i_1 + \gamma_2 i_2$.

A computer program, based on this recursion relation, has been written to calculate the mean duration time at any state in the epidemic process. It uses the counting system described in Section 3 and has the desirable feature that the calculation of the mean duration time of an epidemic in state h requires the computation of mean duration times for only those states j, where $j < h$. [A Fortran listing of the program is available from the first author on request.]

5. SOME NUMERICAL RESULTS

In this section we present the results of an investigation of the relation between the mean duration time and the quantities it depends on, namely, the infection and removal rates and the numbers of susceptibles and infectives in the two populations. Our investigation restricts attention to epidemics starting in a state of the form $(s_1,1;s_2,1)$, i.e., with one initial infective in each population.

We first note that the mean duration time for an epidemic starting in state $(s_1,i_1;s_2,i_2)$ with parameter vector $(\beta_1,\beta_2;\gamma_1,\gamma_2)$ will be c times larger than the mean duration time for an epidemic starting in the same state with parameter vector $(c\beta_1,c\beta_2;c\gamma_1,c\gamma_2)$, for $c > 0$. Hence, only one parameter vector in the family $\{(c\beta_1,c\beta_2;c\gamma_1,c\gamma_2),\ c > 0\}$ need be examined.

For parameter vectors of the form $(\theta,\theta;\theta,\theta)$, the mean duration time increases from its initial value at $s_1 = s_2 = 1$ to a maximum at $s_1 = s_2 = 3$ of 1.52 times the initial value and then decreases to a value at $s_1 = s_2 = 8$ which is 1.05 times the initial value, as illustrated in Figure 1.

[Figure 1 about here.]

To determine why the mean duration time increases and then decreases as $s_1 = s_2$ increases, the parameter vector (0.5,0.0;0.0,0.0) was investigated and the results are presented in Figure 2.

[Figure 2 about here.]

Figure 1. Mean duration time for epidemics starting in state (s_1, 1; s_2, 1) with parameter vector (0.5, 0.5; 0.5, 0.5).

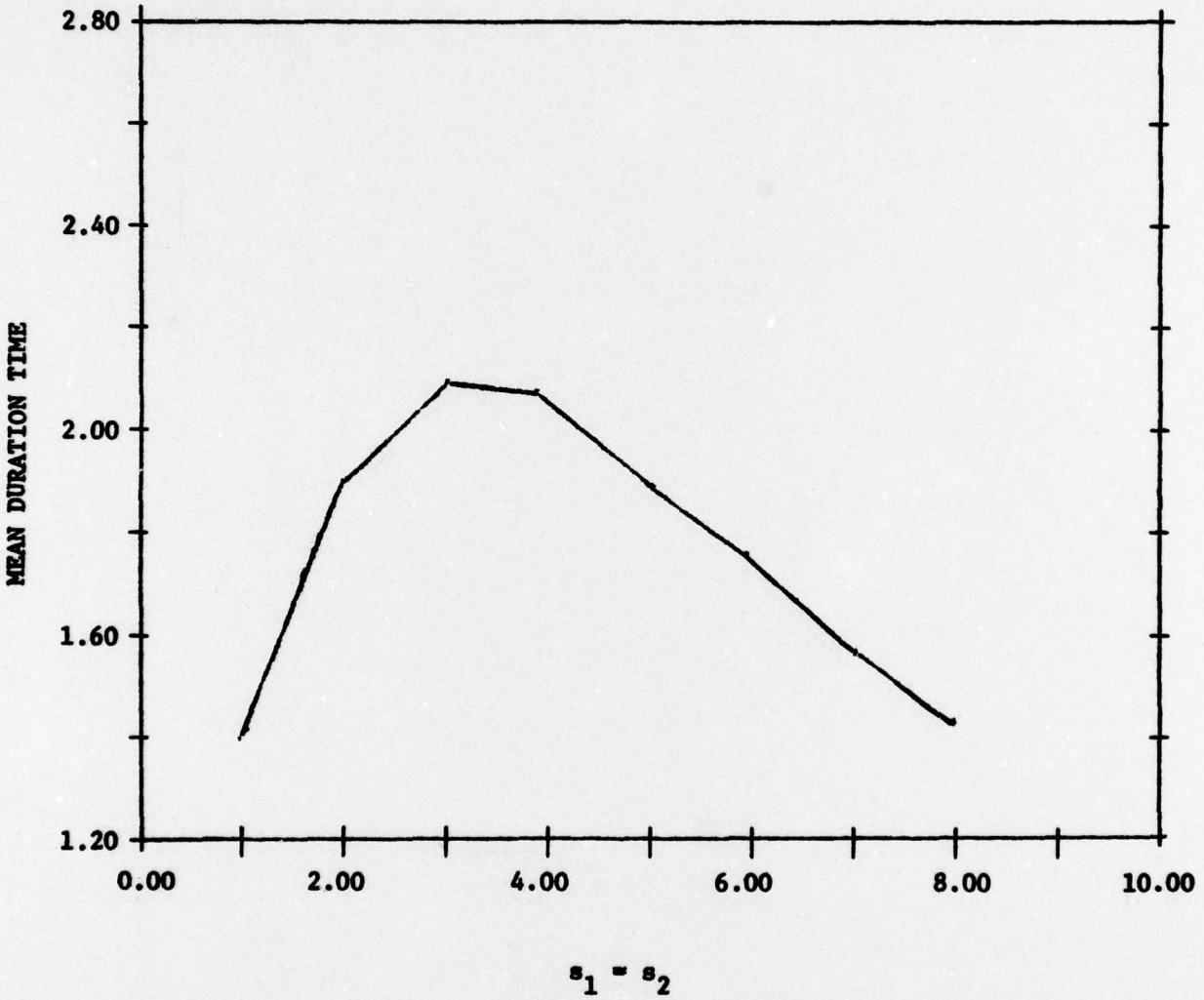
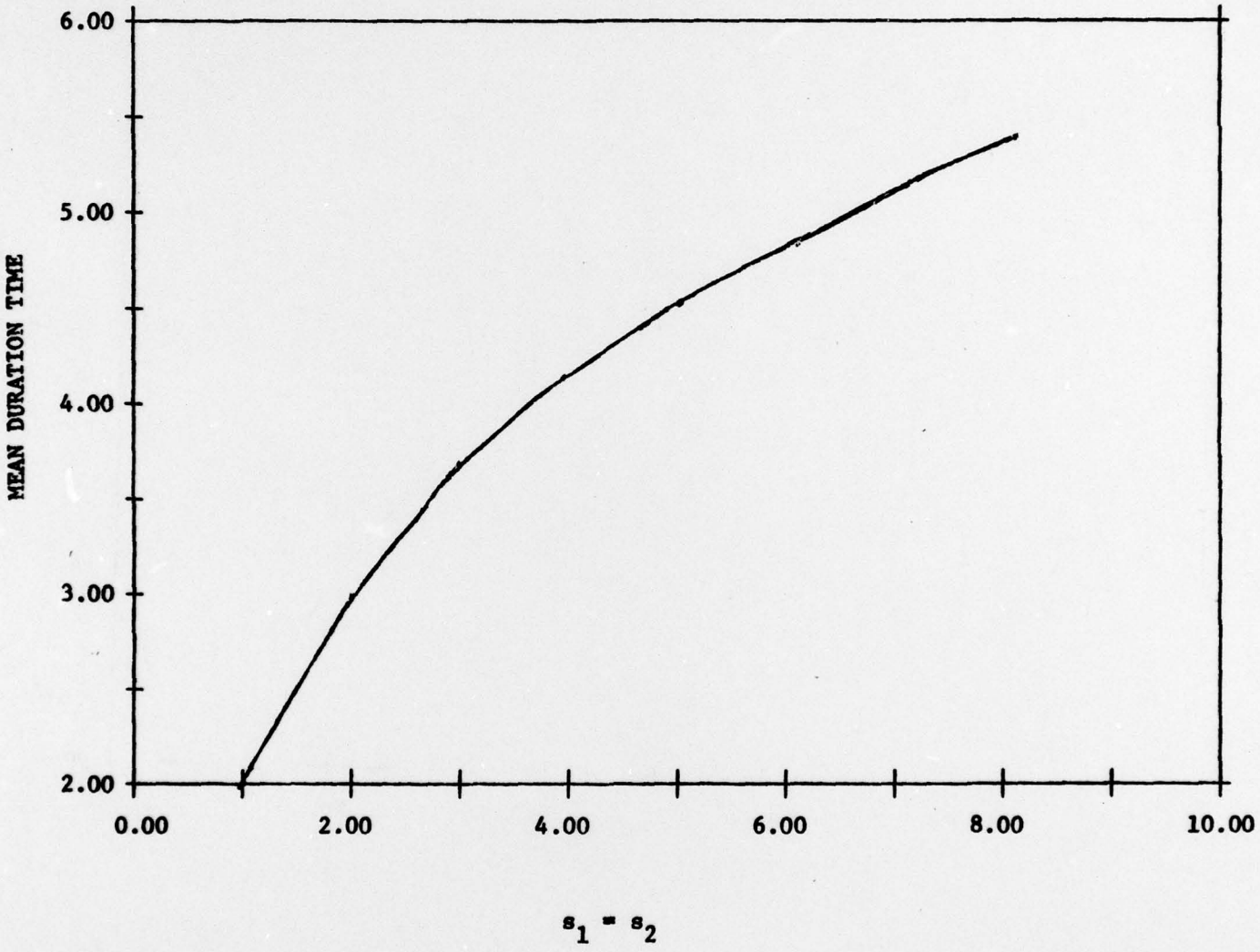


Figure 2. Mean duration time for epidemics starting in state (s_1, 1; s_2, 1) with parameter vector (0.5, 0.0; 0.0, 0.0).



For this parameter configuration, the epidemic can end only if $s_1 = 0$, since any existing infectives are not removed. The consequence of this is that the mean duration time will increase as $s_1 = s_2$ increases since the state (k,1;k,1) decays into (k-1,2;k,1), which has the same mean duration time as (k-1,1;k-1,1) for these parameters.

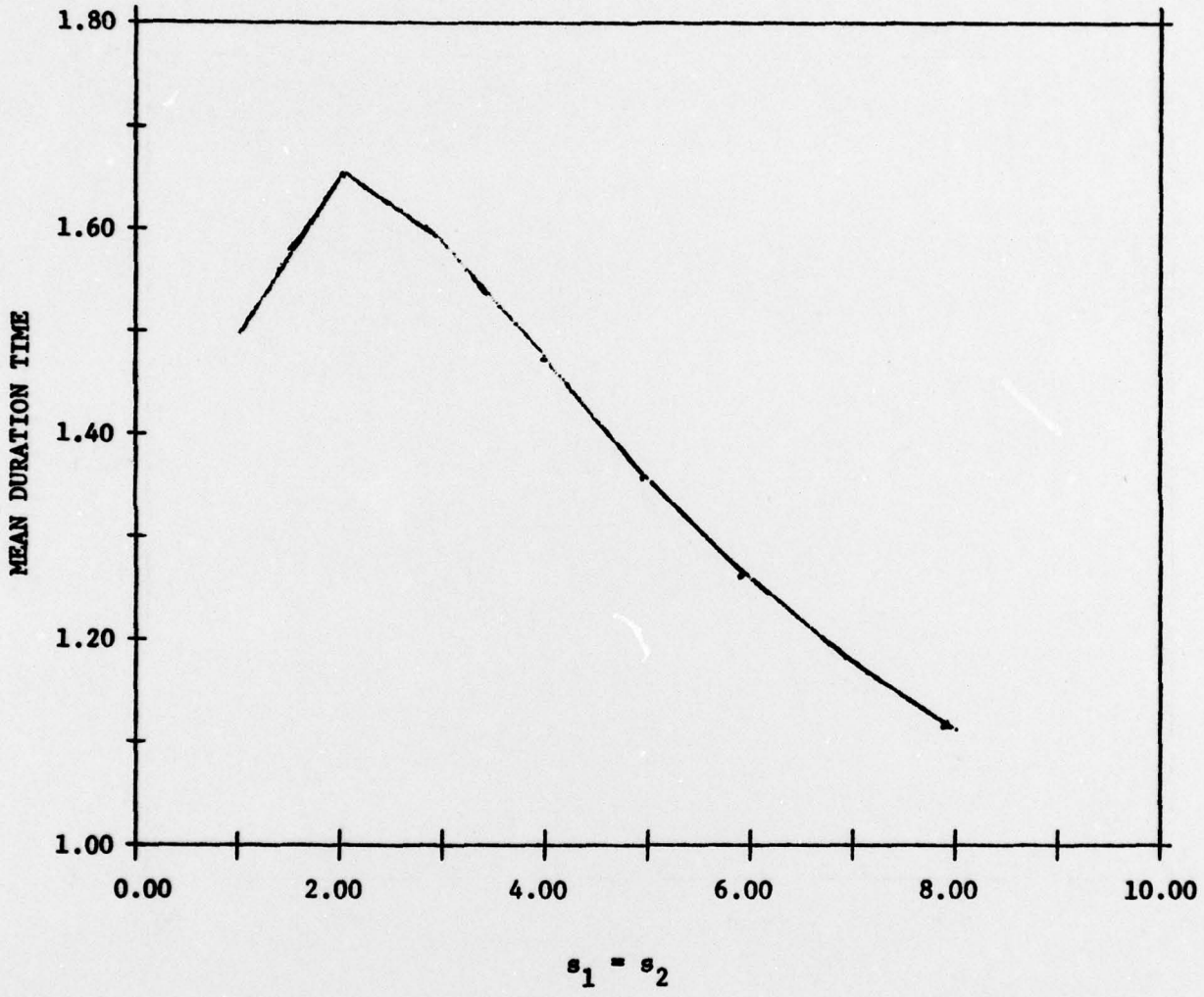
Examination of Figure 3, which presents the mean duration time for an epidemic with parameter vector (0.5,0.5;0.0,0.0), indicates that allowing susceptible carriers to become infected ($\beta_2 > 0$) results in a decrease in the mean duration time, for sufficiently large $s_1 = s_2$, rather than the continued increase as in Figure 2.

[Figure 3 about here.]

With this parameter configuration, the epidemic may terminate only if $s_1 = 0$. The decrease in mean duration time is due to the fact that the rate of transitions of type (i) is $\beta_1 s_1 i_2$. Since $\beta_2 > 0$, i_2 increases and the transition rate tends to be larger than it is in the situation in Figure 2, where i_2 remains constant. Allowing nonzero removal rates does not affect the general shape of the mean duration time curve, as can be seen by comparing Figures 1 and 3.

Thus, the increase and subsequent decrease in the mean duration time observed in Figure 1 can be explained as follows. An epidemic starting in state (1,1;1,1) with parameter vector ($\theta,\theta;\theta,\theta$) is most likely to terminate because s_1 becomes zero. As another host and carrier are added, the time required for s_1 to decrease to zero increases and the epidemic lasts longer. However, the addition of the fourth individuals causes an increase in the hazard rates,

Figure 3. Mean duration time for epidemics starting in state (s_1, 1; s_2, 1) with parameter vector (0.5, 0.5; 0.0, 0.0).



which more than offsets the additional time required to remove the fourth susceptible host. Thus, the mean duration time of an epidemic in state (4,1;4,1) is less than that of an epidemic in state (3,1;3,1).

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20. ABSTRACT

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